FDA TSE Advisory Committee
Rockville, Maryland
June 26-27, 2002

Disinfection and Sterilization of TSE Contaminated Surgical Instruments

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Main Points

- Susceptibility to inactivation of TSE infectivity is within normal range for viruses and spores.
- TSE infectivity is nevertheless resistant to disinfection and/or sterilization.
- Resistance to inactivation is not due to failure of the inactivants but to inadequate exposure to them.

Sources

- Rohwer, R.G. Virus-Like Sensitivity of the Scrapie Agent to Heat Inactivation. (1984) Science 223, 600-602.
- Rohwer, R.G. Scrapie Infectious Agent is Virus-like in size and susceptibility to inactivation. (1984) Nature 308, 658-662.
- Rohwer, R.G. The Scrapie Agent: "A Virus by Any Other Name." (1991) Current Topics in Microbiology and Immunology, 172, 195-232.

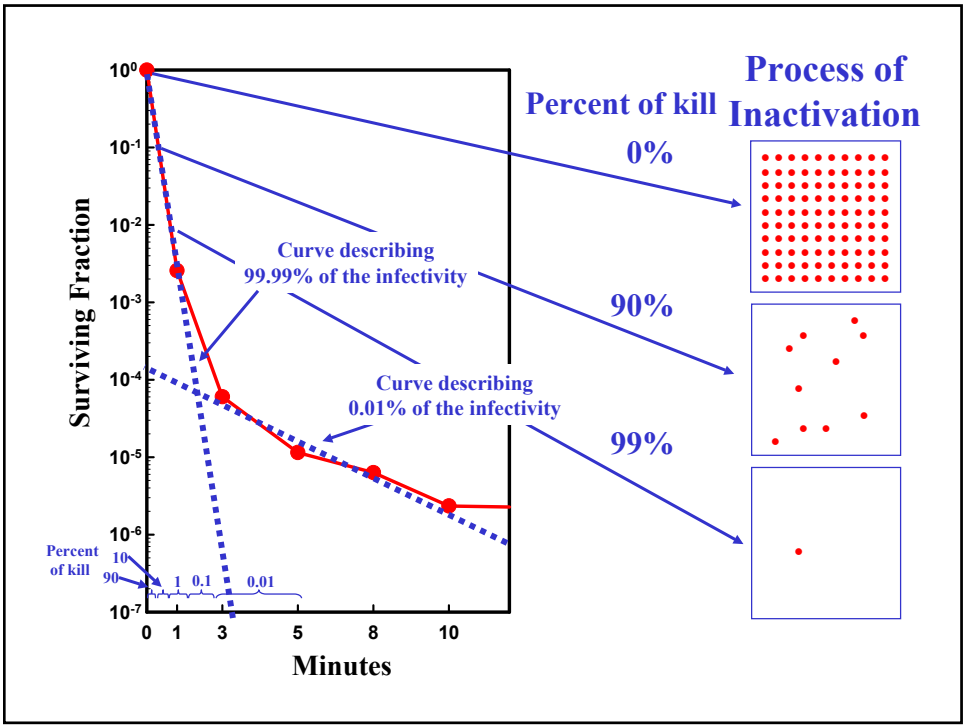
Resources

WHO/CDS/CSR/APH/2000.3

WHO Infection Control Guidelines for Transmissible Spongiform Encephalopathies

Report of a WHO Consultation
Geneva, Switzerland, 23 - 26 March 1999

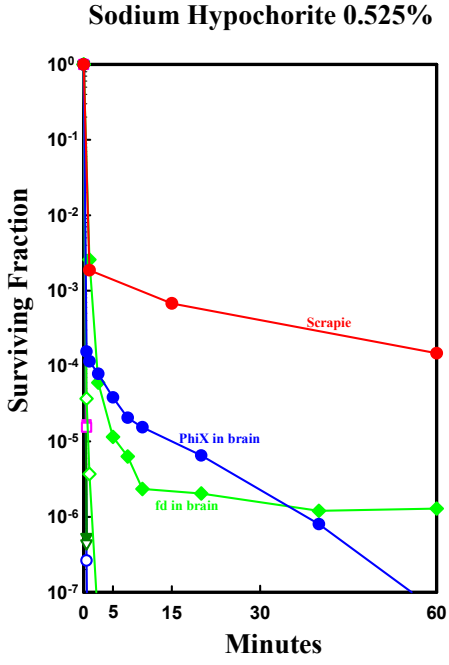
http://www.who.int/emc-documents/tse/whocdscsraph2003c.html



Comparing Agent Properties

- The properties intrinsic to the agent are reflected in the initial rate of inactivation
  - Vast majority is being inactivated
  - Interpretation is less complex
- The size of the residual fraction is a complex function of environmental parameters and can not be used to compare the intrinsic sensitivities of agent strains.

Chemical Inactivation



Inactivation of TSE Infectivity by NaOH
Log_{10} Titer Lost

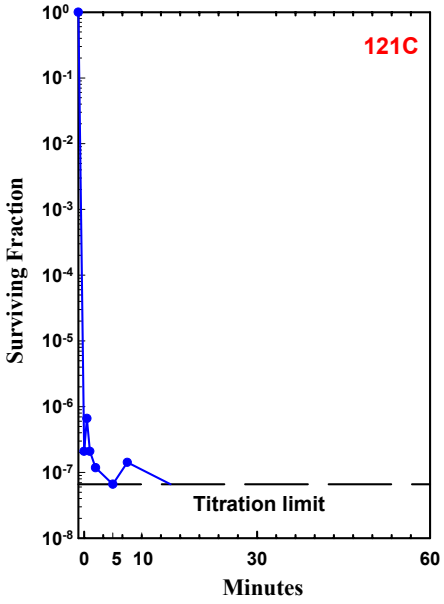
CONCENTRATION	CJD		263K SCRAPIE	
	15 min.	60 min	15 min	60 min
0.01N	-	1.0	0	1.0
0.1 N	4.8	4.8	5.0	6.0
1.0N	4.5	>5.0	6.0	>6.8
0.25 N	4.7	4.8		
0.25 N + 1%SDS	>4.0	4.0		

(Brown, P.; Rohwer, R.G.; Gajdusek, D.C. (1986) Newer data on the inactivation of scrapie virus or Creutzfeldt-Jakob disease virus in brain tissue. J. Infect. Dis. 153:1145-1148.)

AUTHOR	CONC.	TIME	TEMP.	LOG REDUCTION
Haig & Clarke	pH 9.8	overnight	4°C	0.5
Mould et al.	pH 10.5	34 hrs	2 °C	0.7-1.4
Millson & Hunter	5N			"dramatic"
Prusiner et al.	0.3N	18 hrs.	4 °C	5
in 320 mM sucrose	0.3N	2 hrs.	30 °C	5
	0.3N	1hrs.	70 °C	4
	0.3N	8hrs.	4 °C	5
after enzymes	0.3N	3hrs.	37 °C	>6
	0.3N	1hr.	70 °C	>5
storage	0.3N	14-21 days	-20 °C	complete
bicarbonate	pH 9.8	24 hrs.	-	2
	1N	24 hrs.	25 °C	activity
Diener et al.	PH 9.0	1 hr.	4 °C	0
	pH 10	1 hr.	4°C	5
Brown, Rohwer et al.	1N	1 hr.	22°C	≥5.5
	0.1N	1 hr.	22°C	≥5.5
Ammonia	1N	1 hr.	22°C	1
Tateishi et al.	1N	2 hrs.		some
(dialysis)	2N	2 hrs.		activity
(dialysis)	0.25N	2hrs.	22°C	some
	1N	2 hrs.	22 °C	activity
	2N	2 hrs.	22 °C	
Tamai et al.	1N	1 hr.	22 °C	some activity
Diringer et al.	1N	1 hr.	22 °C	1 out of 40
	0.1N	1 hr.	22 °C	died
Taguchi et al.	1N	1 hr.	22 °C	some activity
Di Martino et al.	1N	1 hr	22 °C	6
(aqueous methanol)	pH 12	4 hrs.	40 °C	complete
Earnst et al.	1N	"gave	large reductions"	

Heat Inactivation

Wet Heat Inactivation at 121°C

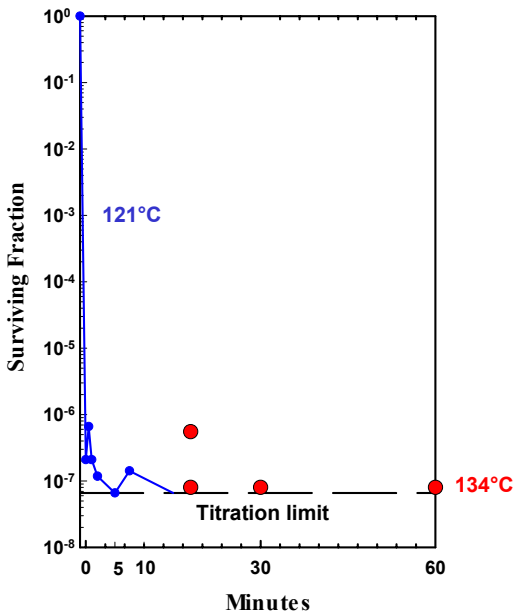


Taylor Steam Inactivations

D.M. Taylor et al. (1994) Arch. Virol. 139:313-326

Porous Load Autoclave	
Condition	**infected/total**
Untreated	19/19
134°C 18min.	4/13
134°C 30min.	4/26
134°C 60min.	14/22
134° - 138°C 18min.	19/19

Heat Inactivations



Dry Heat Inactivation

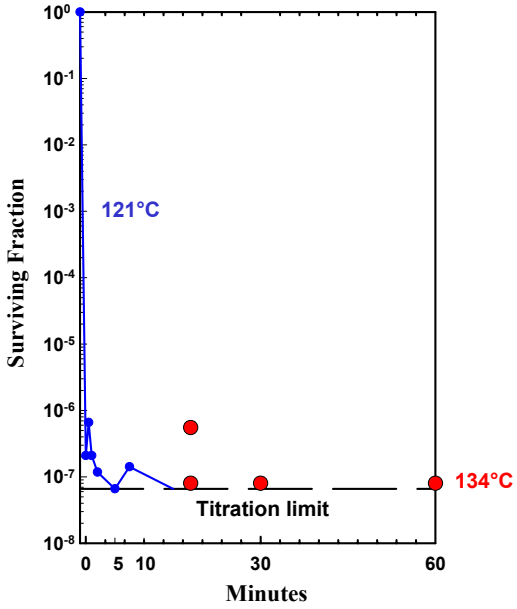
Condition	Log_{10} Reductions Whole Brain
Untreated	0
160°C 10m	2-3
160°C 60m	3-4
360°C 60m	9

P. Brown & D.C. Gajdusek (1991) Brain Research Rev. 16:100-103.

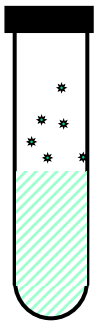
Temperature insensitivity of residual infectivity

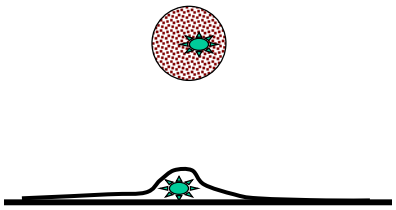
- 132ºC is a significantly higher temperature than 121ºC for a steam sterilization where inactivation takes place in minutes.
- 132ºC is only incrementally more effective than 121ºC for a dry heat sterilization where inactivation takes days at those temperatures.

Heat Inactivations



If the reagent can't reach it it can't kill it.





Brain is 50% fat.
Oxidized fats are varnishes and plastics.

Steam Sterilization

- Not intrinsically resistant
- The problem is with delivery of inactivant

Sterilization

- Prevent drying
  - —Immerse in water prior to and during steam sterilization
- Combine two or more methods
  - —Heat and hydroxide

Effective Delivery

- Well dispersed
  - —Surfactants
  - —Homogenization
- Eliminate Sanctuaries
  - —Agitation
- Refinement
  - —Reduces potential for protective associations

WHO/CDS/CSR/APH/2000.3

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World Health Organization
Department of Communicable Disease Surveillance and Response

Table 5 General measures for cleaning instruments and environment

1.	Instruments should be kept moist until cleaned and decontaminated.
2.	Instruments should be cleaned as soon as possible after use to minimize drying of tissues, blood and body fluids onto the item.
3.	Avoid mixing instruments used on no detectable infectivity tissues with those used on high and low infectivity tissues.
4.	Recycle durable items for re-use only after TSE decontamination by methods found in Section 6 and Annex III.
5.	Instruments to be cleaned in automated mechanical processors must be decontaminated by methods described in Section 6 and Annex III before processing through these machines, and the washers (or other equipment) should be run through an empty cycle before any further routine use.
6.	Cover work surfaces with disposable material, which can then be removed and incinerated; otherwise clean and decontaminate underlying surfaces thoroughly using recommended decontamination procedures in Section 6 and Annex III.
7.	Be familiar with and observe safety guidelines when working with hazardous chemicals such as NaOH and bleach.
8.	Observe manufacturers' recommendations regarding care and maintenance of equipment.

1. Incineration

1. Use for all disposable instruments, materials, and wastes.
2. Preferred method for all instruments exposed to high infectivity tissues.

2. Autoclave/chemical methods for heat-resistant instruments

1. Immerse in sodium hydroxide (NaOH)[20] and heat in a gravity displacement autoclave at 121°C for 30 min; clean; rinse in water and subject to routine sterilization.
2. Immerse in NaOH or sodium hypochlorite[21] for 1 hr; transfer instruments to water; heat in a gravity displacement autoclave at 121°C for 1 hr; clean and subject to routine sterilization.
3. Immerse in NaOH or sodium hypochlorite for 1 hr.; remove and rinse in water, then transfer to open pan and heat in a gravity displacement (121°C) or porous load (134°C) autoclave for 1 hr.; clean and subject to routine sterilization.
4. Immerse in NaOH and boil for 10 min at atmospheric pressure; clean, rinse in water and subject to routine sterilization.
5. Immerse in sodium hypochlorite (preferred) or NaOH (alternative) at ambient temperature for 1 hr; clean; rinse in water and subject to routine sterilization. Autoclave at 134°C for 18 minutes.
6. Autoclave at 134°C for 18 minutes.[22]

[20] Unless otherwise noted, the recommended concentration is 1N NaOH.
[21] Unless otherwise noted, the recommended concentration is 20 000 ppm available chlorine.
[22] In worse-case scenarios (brain tissue bake-dried on to surfaces) infectivity will be largely but not completely removed.

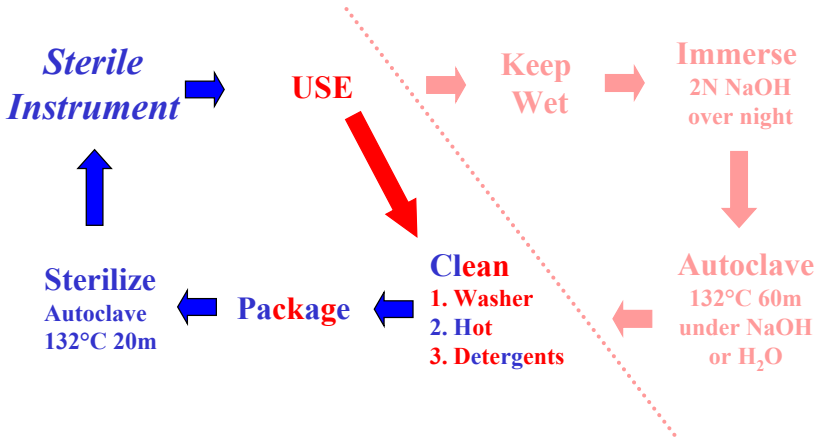
Disinfection and sterilization in the TSE laboratory

Experimental Evidence of Effectiveness

- **Using instruments from the reuse pool cleaned and sterilized as stated:**
  - **No infections among hundreds of animals inoculated with blood fractions depleted of infectivity.**
  - **No infections among hundreds of animals inoculated with blood collected at early times in the infection.**

UNPUBLISHED DATA

Cleaning and sterilization in the hospital



Hospital Cleaning before Sterilization

- Overwhelms all other contamination issues
- Creates a secondary decontamination problem
  - Decontamination of washer
  - Decontamination of waste
- Can not be presumed to be adequate
  - Must be validated

Hotel Dieu Grace – Windsor Ontario

- Could not identify exposed instruments
- Commingled general pool
- Sterilized entire pool at once
- No test sample(s)
- Autoclave in 1N NaOH
- Electrolysis
- Fumes?
- Destruction estimated at $10 m.

Hotel Dieu Grace – Windsor Ontario

- Complete details have not been released
- Apparent chemical incompatibilities
- WHO Guidelines are based on laboratory experience
- Need to develop and validate procedures that work in a hospital setting
- The instrument washer was not considered a source of vulnerability
  - Sterilization of the instruments is pointless without sterilization of the washer
  - If the washer is itself sterilizing, then resterilization of the instruments was unnecessary.

Practical Issues of Infection Control of CJD

Most of the Exposure is from Incubating Cases

- Can identify only a minor proportion
  - Familial, iatragenic and geographic exposures
- Can not identify incubating sporadic cases
- It is pointless to implement measures that attempt to reduce the risk from known cases to below the irreducible risk from unidentifiable cases.
- Unless apply a uniform higher standard

The End